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December 1961

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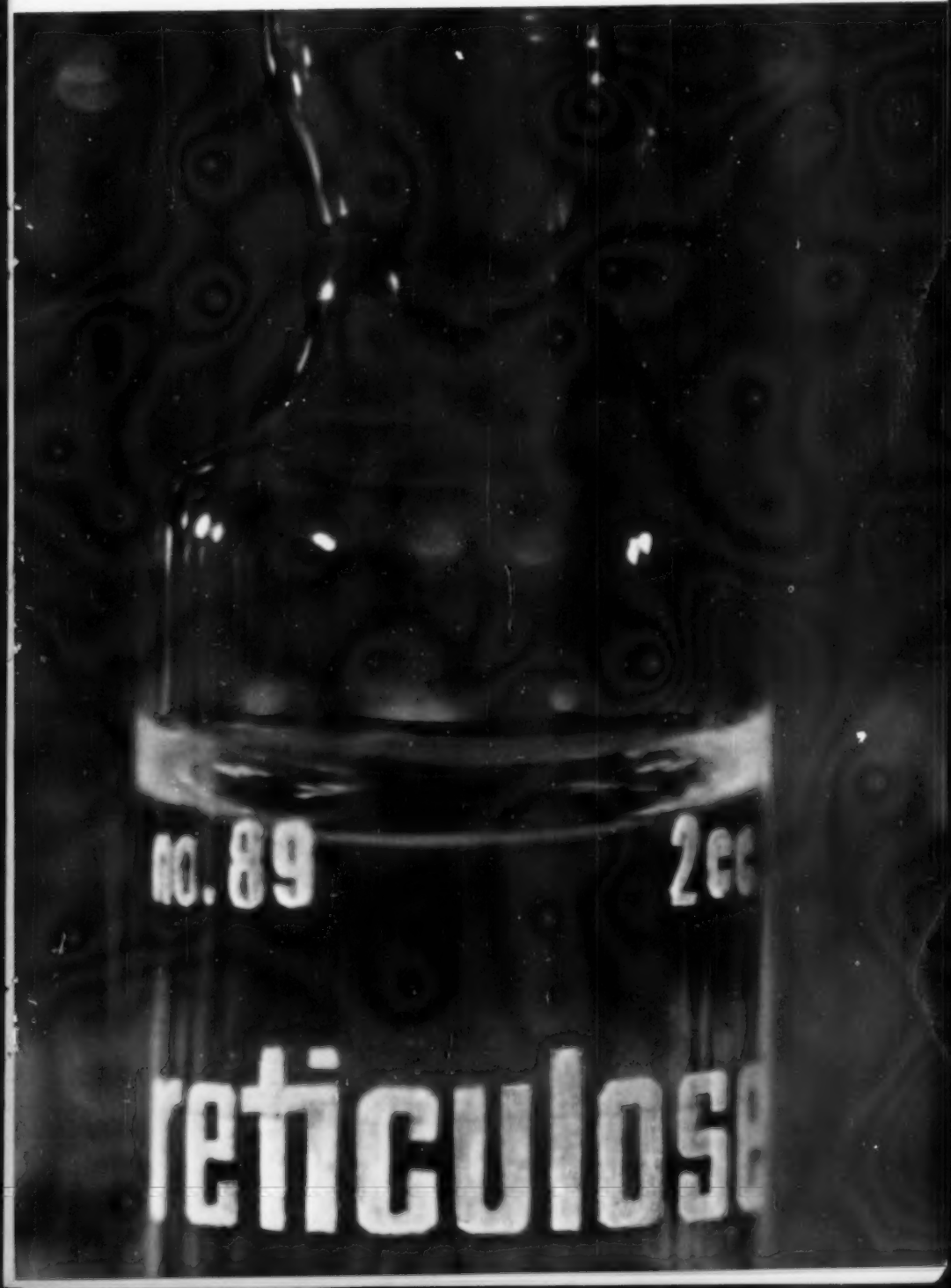

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Bibliography: 1. Anderson, R. H., Thompson, R. M., Treatment of Viral Syndromes, Va. Med. Mo. Vol. 84-347 353, 7-57. 2. Scientific Exhibit, Va. State Medical Soc., Washington, D.C. Oct. 1957. 3. Symposium Viral Diseases, Miami, Fla. September, 1960. 4. Reynolds, R. M., Vaccinia, Archives of Pediatrics, Vol. 77 No. 10 Oct. 1960. 5. Wegryn, S. R., Marks, Jr. R. A., Baugh, J. R., Herpes Gestationis, American Journal Ob. and Gyn., Vol. 79 Apr. 1960.

Literature is available upon request.

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References: 1. Freedman, A. M.: Pediat. Clin. North America *5*:573 (Aug.) 1958. 2. Nathan, L. A., and Andelman, M. B.: Illinois M. J. *112*:171 (Oct.) 1957. 3. Santos, I. M. H., and Unger, L.: Ann. Allergy *18*:179 (Feb.) 1960. 4. Litchfield, H. R.: New York J. Med. *60*:518 (Feb. 15) 1960.

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ARCHIVES OF PEDIATRICS

ALBRO C. GAYLOR, *Publisher*
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Vol. 78 No. 12

December 1961

CONTENTS

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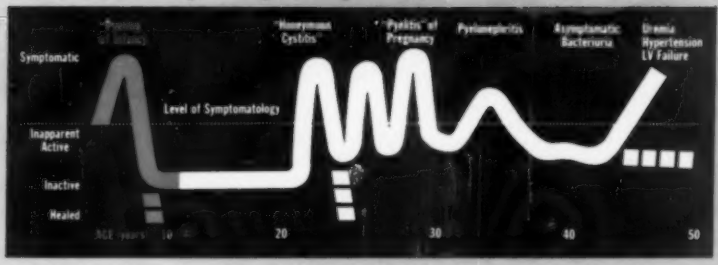
Natural History of Pyelonephritis



"... the theme that runs through the carefully taken history of most uremic patients with chronic pyelonephritis—the burning on urination of infancy, the chills and fever in childhood, the 'honeymoon' pyelitis, the recurrent urethritis treated so well and often locally—and yet the termination in uremia."[1]

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REFERENCES: 1. Birchall, R.: Am. Practit. *11*:918, 1960. 2. Stevenson, S. S.: J. Louisiana Med. Soc. *110*:219, 1958. 3. Marshall, M., Jr.: J. Kentucky Med. Assoc. *59*:35, 1961. 4. Johnson, S. H., III, and Marshall, M., Jr.: J. Urol. *82*:162, 1959.

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1. Newsome, C. K.: The challenge of triacetyloleandomycin in pediatric infections, J. Indiana M.A., *53*:1131 (June) 1960.

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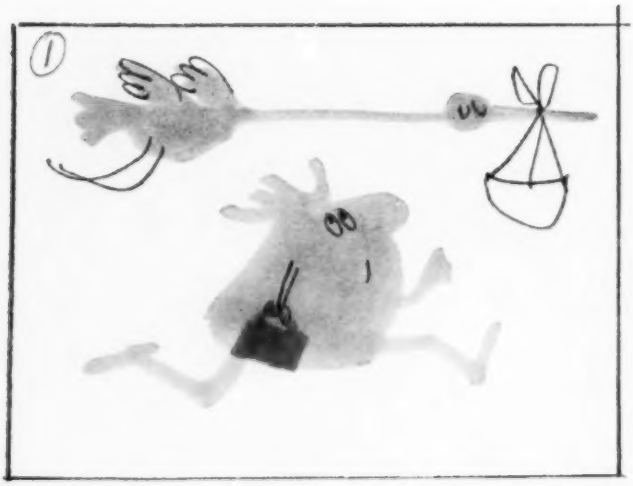

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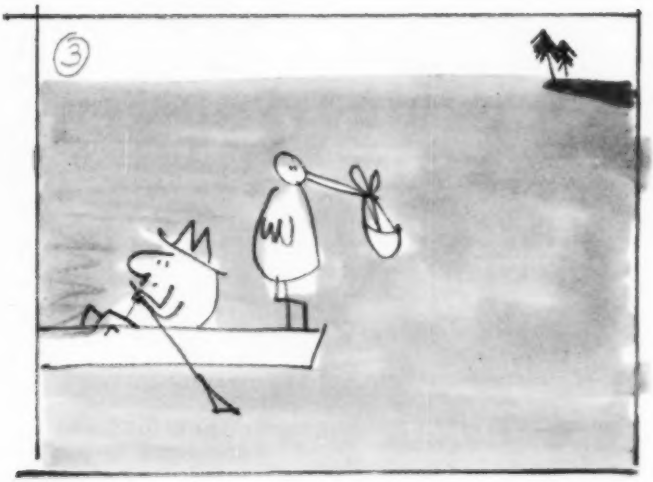

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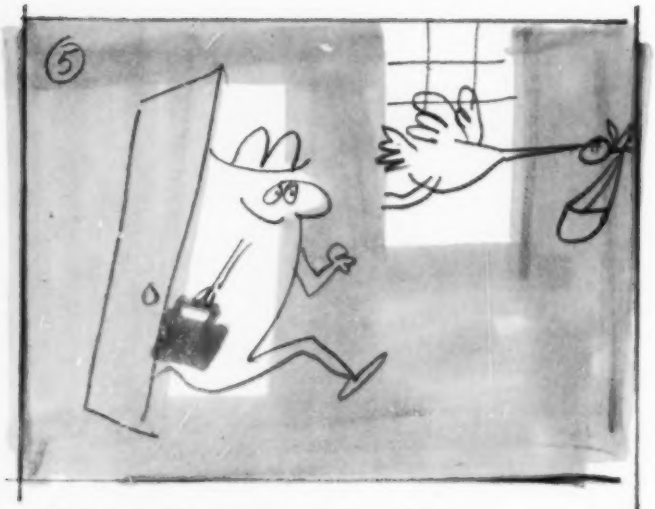

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Fluoride (as sodium fluoride)	0.5 mg.

Indications: As an aid in the prevention of dental caries and in the prophylaxis and treatment of deficiencies of Vitamins A, C, D, and B_6.

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May be administered by dropping directly on the tongue or by mixing with water, milk, fruit juice, or food.

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Supply: 15, 30, and 50 cc. plastic bottles with a plastic, calibrated (0.6 cc.) dropper. Available on prescription only.

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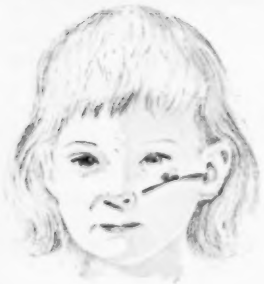

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1. Budetti, J. A., and Seydell, E. M.: *J. Kansas M. Soc.* 57:59, Feb., 1956.
2. Soss, T. L., in Collect. Letters, Internat. Cor. Soc., Ophthalmologists & Otolaryngologists 3:177, Dec. 15, 1958.

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The Cover . . .

The University of Oklahoma Medical Center, is pictured against a backdrop of the downtown Oklahoma City business section. The complex includes the Oklahoma City Veterans Administration Hospital (lower center) and, to the right of the VA Hospital, the Oklahoma Medical Research Foundation, the University of Oklahoma Speech and Hearing Center, and the Basic Science building of the University of Oklahoma School of Medicine. Across the street and left of the VA Hospital, is Children's Memorial Hospital, and to the right are the University of Oklahoma School of Nursing, the nine-story University Outpatients unit and main University Hospital. The four-story structure immediately in front of the University Hospital is a new research building.

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Children from 6 months to 1 year, 1/4 teaspoon; 1 to 3 years, 1/2 to 1 teaspoon; 3 to 6 years, 1 to 2 teaspoons; 6 to 12 years, 2 teaspoons. Every four to six hours as needed.

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Structural Basis for Athetosis in Cerebral Palsied Children*†

A PRELIMINARY REPORT

CYRIL B. COURVILLE, M.D.
California

SYMPTOMS assumed to be due to a dysfunction of the extrapyramidal system occur frequently in cerebral palsied patients, so much so that a separate clinical classification is usually made. Such persons are usually described as presenting an athetoid or choreo-athetoid syndrome. However, dystonia is also occasionally seen in such patients. Rigidity as distinguished from spasticity as a ganglionic manifestation further alters the clinical picture in many instances.

From a clinical viewpoint these symptoms are to be distinguished from the various syndromes coming on in later life (Sydenham's or Huntington's chorea, Parkinsonism of various etiologies, hemiballismus, etc.). In addition, the association of these specific symptoms with motor or cerebellar phenomena often indicates a complex suggesting a more widespread involvement of portions of the brain other than the basal ganglia. One may therefore expect instances of "pure" or almost pure ganglionic syndromes as well as instances in which such manifestations are minimal and more or less obscured by other motor symptomatology.

Pathologic Physiology of Striatal Hyperkinetic Phenomena.—An understanding of clinical symptoms presumed to result from disorders of the corpus striatum and allied structures has been difficult to attain in terms of structural change. This is natural, as there have been about as many schemata of the nervous connections of the central gray masses as there have been independent investigations of the problem. Moreover, there has not been an agreement as to what types of cells, large or small, are involved in the various structures which have been damaged. There have been suggestive manifestations observed in patients whose brain showed no significant post mortem changes, and there have been

* From the Cajal Laboratory of Neuropathology, Los Angeles County Hospital, and the Division of Nervous Diseases (Neurology), College of Medical Evangelists, Los Angeles, California.
† The research upon which this contribution was based was supported by a grant (B 1248) of the National Institute of Neurological Diseases and Blindness, Bethesda, Maryland.

other cases with gross lesions found at autopsy who were apparently entirely free of any typical striatal symptoms during life. All such observations demand a critical approach to any attempt to associate symptoms and structural changes in this group of palsied persons.

CLINICAL ASPECTS OF STRIATAL PHENOMENA

In view of the uncertainty of the source of the individual symptoms believed to be of striatal origin ("striatal" referring not only to the corpus striatum itself but also to the ganglionic masses associated with it such as the globus pallidus, the substantia nigra, the corpus subthalamicum [Luys], the red nucleus, and even some thalamic nuclei), it is necessary to define just what clinical manifestations are to be anticipated. It is recognized that the most common symptom referrable to the basal ganglia is that of a fine rhythmic *tremor* such as is seen in cases of Parkinsonism. This tremor may or may not be associated with variable degrees of *rigidity*, another manifestation of damage to basal ganglia. However, tremor of this type is rarely observed as the principal striatal symptom in patients with cerebral palsy.

Another characteristic symptom is that of irregular jerking movements of the face or extremities. These movements are irregular in sequence, duration, and are usually described as purposeless movements. This symptom is commonly designated as a *choreaform movement*. A symptom described as *athetosis* and perhaps more commonly seen in cerebral palsied children is a continuous irregular writhing movement, more or less constantly present during the waking hours of the patient. This movement may be exaggerated by emotional or physical tension. Still another symptom, but one only rarely seen in cerebral palsied children, is that of *dystonia*. This is an irregular twisting movement of the extremities of one side or both sides of the body, usually occurring as a torsion spasm. Whether unilateral or bilateral, such twisting movements occur about the long axis of the member involved, and are often complicated by tortion movements of the trunk itself. *Hemiballismus* is more often the result of an acute vascular lesion and is therefore not a part of this problem in cerebral palsy.

These irregular hyperkinetic movements in cases of cerebral palsy are sometimes so pronounced as to constitute the essential if not the entire element of the total clinical picture. On the other hand, minor movements are often obscured by a more pronounced paralysis of the members involved. Therefore, a mixed or complex

picture in which paralytic and hyperkinetic phenomena are intermingled is not uncommon. Under such circumstances it is difficult to distinguish the hyperkinetic activity which results from damage to the pyramidal system or from a dysfunction of the cerebellum.

STRIATAL LESIONS IN CASES OF CEREBRAL PALSY

It is important to stress the fact that in some cases with outstanding striatal phenomena, no gross lesions whatever are found at autopsy. Paradoxically, one may find at autopsy very severe lesions of the corpus striatum or any of its nuclear masses without any clinical evidence of striatal character having been noted during life. On the other hand, one may find commensurate with the characteristic symptoms some alterations, gross or microscopic, in these cases.

In our series of autopsied cases of cerebral palsy studied at the Cajal Laboratory there are now available records of 160 examples of the changes found in the brain.

Types of alterations in the basal ganglia were recorded as follows:

1. The basal ganglia may appear grossly normal in spite of the fact that the patient may have had some suggestive corpus striatal phenomena.
2. There may be an atrophy of one or more of the basal ganglia evidently due to loss of nerve cells in these structures.
3. At times microcystic degeneration associated with a profound gliosis may also occur. Several small sharply circumscribed cysts are found in a greatly shrunken and gliosed lenti' 'ar nucleus.
4. The lenticular nucleus, either in whole or in part (putamen or globus pallidus), may also show gross cystic degeneration, being occupied by a single smooth-walled cavitation.
5. The entire structure may be necrotic, evidently due to some profound impairment of circulation.
6. In some cases there is a peculiar mottling of the caudate or lenticular nuclei or thalamus due to the hypertrophy of bundles of white fibers (status marmoratus or "marbled state").
7. A loss of the myelinated fibers may also be present in the external capsule and the putamen, evidently interfering with its function (status dysmyelinisatus). Each of these situations will be discussed briefly in the following section.

"Normal" Basal Ganglia. In some cases of cerebral palsy one finds at autopsy what appears to be a perfectly normal brain.

The structures associated with the pyramidal or the extrapyramidal system are likewise not appreciably altered. It is evident, therefore, that under these circumstances any disturbance in function must present some alteration in the finer structure or function of nerve cells or their connections. This may also be true in dyskinetic phenomena considered to be of striatal origin. However, one must assume that some disturbance in structure of the cells does exist to explain the phenomena even though it may be extremely difficult to pinpoint the focus of the disturbance.

Atrophy of the Basal Ganglia. This is somewhat more common and is likely to be found in the hemiatrophies or the irregular atrophies of the brain in cases of cerebral palsy. One may find in the smaller hemisphere (hemiatrophy) a caudate nucleus, lenticular nucleus, or even a thalamus which is reduced in size. Once in awhile the situation is paradoxical and one finds a smaller than normal lenticular nucleus with a normal sized or perhaps even larger thalamus than its fellow (fig. 1). One may find also a shrinkage in the size of the basal ganglia or at least those entering into the structure of the corpus striatum (caudate nucleus and putamen of the lenticular nucleus) even though the hemisphere itself does not appear to be particularly atrophic. In these cases one would more likely suspect some dysfunction in the realm of the extrapyramidal system, although this is not absolutely the rule.

In cases of atrophy of any of the nuclei one would anticipate that either the large or small cells constituting these nuclei or their connections have undergone some degree of deterioration. It is otherwise difficult to account for shrinkage of these physical structures. A careful study of these areas with appropriate staining methods (Nissl, Bielschowsky, or reduced silver) will often show a decrease in population of the large or small nerve cells as well as some reduction in number and complexity of their constituent nerve fiber connection. Indirectly one may also find with the gold sublimate method or the Holzer stain for astrocytic fibrils a secondary gliosis suggesting that there has been a change in the interstitial as well as in the parenchymatous elements.

Microcystic Degeneration. This type of change seems to be rather rare. I have found it only once in my series of 160 cases. The lenticular nucleus in this case was shrunken overall and obviously had undergone a secondary gliosis, for it was hard and fibrous in texture. In the substance of the nucleus were several small, sharply circumscribed cystic spaces quite evident on cross

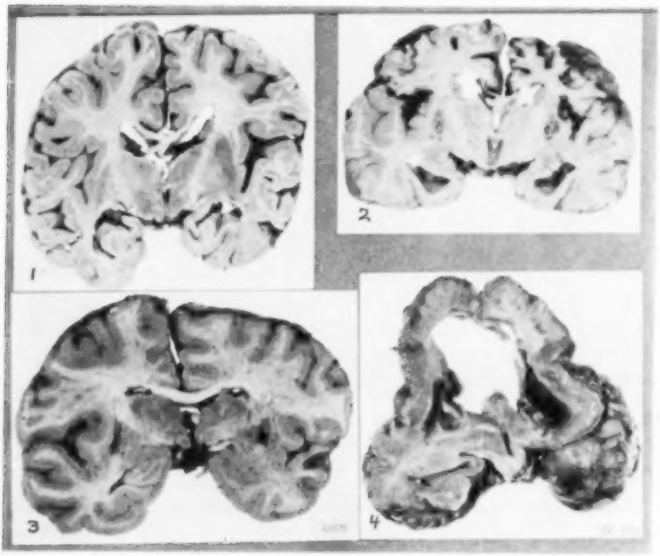

Fig. 1. Cross section of brain of palsied child showing atrophy of left thalamus with compensatory hypertrophy of left lenticular nucleus. This was the brain of an 8-year-old boy who early showed uncontrolled movements later obscured by spastic quadriplegia in extension but with flexion contractions of upper extremities.

Fig. 2. Cross section of brain showing nodular cortical atrophy and bilateral microcystic degeneration of the putamen in a case of spastic and mentally deficient 3-year-old boy.

Fig. 3. Gross bilateral cystic degeneration of putamen and minor atrophy of the thalami in an adult with left-sided spastic paralysis and torticollis since age 6 years. No other symptoms of ganglionic disease.

Fig. 4. Widespread cortical and ganglionic softening (caudate and lenticular nuclei) in a 16-month-old male infant, spastic and epileptic since birth.

section (see fig. 2). This suggested that there had been some selective damage to the lenticular nucleus often associated with injury to the regional cortex as is true in this case. The gross specimen presented a classical picture of lobar sclerosis with atrophy and gliotic change in the upper convolutions, as is shown in this picture. In this patient, however, there was no significant change in the functions of the corpus striatum. If any suggestive symptoms occurred they were overwhelmed by the profound degree of paraplegia present.

Gross Cystic Degeneration. The occurrence of a smooth-walled cystic cavity within any nuclear mass, particularly the putamen or globus pallidus, suggests that the original process may have

been asphyxial in character, for such cystic cavities strongly resemble those found after severe and fatal exposure to carbon monoxide (fig. 3). This detail will be considered in a subsequent section. Such cystic changes may or may not be associated with other cortical defects or alterations in the regional nervous connections.

Total Necrosis of the Lenticular Nucleus. This is likewise a relatively rare change—a single case being found in my series. There was an associated profound softening of the cortex of most of the cerebral hemisphere, particularly that supplied by the anterior and middle cerebral arteries (fig. 4). The association of these two profound changes indicates that the cause of both must lie in some profound impairment of circulation, one often initiated before the birth of the child. In this case there was no hyperkinetic phenomena observed, although there was marked widespread rigidity in extension several months before the infant's death.

Status Marmoratus. This condition has been known for some time, having been the subject of considerable study by the Vogts. These investigators thought this peculiar change to be responsible for choreo-athetosis found in these cases. The cause of this disease was variously interpreted by them. At first, they thought that in view of the history of anoxia at birth in some of their cases, paranatal asphyxia was indeed the cause of the disorder. They later suggested, however, that there was some other background, such as a congenital malformation, for the disease. It is of interest to know that a considerable number of patients who die with this disorder have had a difficult delivery. Some have interpreted the occurrence of this disorder as due to the result of a traumatic episode at birth without considering the possibility of an asphyxial process going on. The direct etiology will be considered in a subsequent section.

The accompanying illustration (fig. 5) gives a fairly classical picture of the presence of numerous hypertrophied bundles of myelinated nerve fibers affecting the lateral aspects of the thalamus in a patient having classical symptoms of choreo-athetosis.

Status Dysmyelinisatus. We also have a situation in which there is a degeneration of the myelinated nerve fibers in the external capsule and in the putamen (fig. 6). In this case there was a clinical picture of dystonia rather than of choreo-athetosis. However, in some reported cases athetosis is present instead. In this

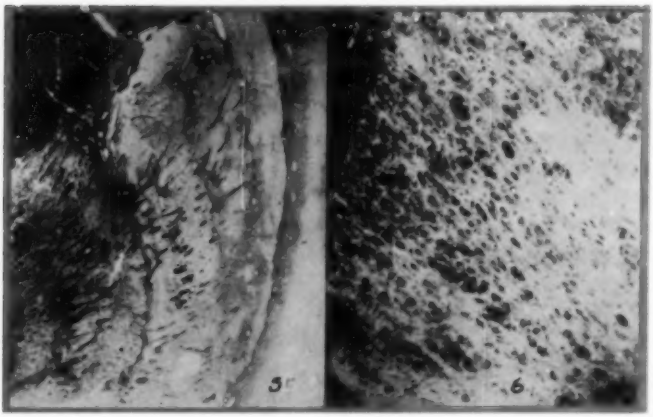

Fig. 5. Characteristic excessive patchy myelination (status marmoratus) in thalamus of a 33-year-old male individual with dystonia musculorum deformans and gross truncal deformity and spastic paralysis with contractures of all four extremities since infancy.

Fig. 6. Demyelination of the external capsule and adjacent part of putamen in a 27-year-old male patient with double athetosis, spastic paraplegia, and convulsions since infancy.

instance one finds a more definite connection with the possibility of paranatal asphyxia; this pathological picture can be duplicated in many cases of severe asphyxia of later life which survive for an interval sufficiently long for degeneration to occur in these fibers. This has been shown in our own cases of asphyxia from various causes.

With these different types of lesions found in the brain in cases of cerebral palsy, we are now prepared to consider the pathogenesis of these various disorders.

PATHOGENETIC PROCESSES RESPONSIBLE FOR DAMAGE TO THE CORPUS STRIATUM

A survey of the causes of striatal damage in later life makes it clear that a number of pathological processes may damage these structures. One must consider the possibility of infectious disorders in the form of the primary toxic effects of endogenous or exogenous bacterial toxins such as act in Sydenham's chorea. This disorder is usually believed to be secondary to Streptococcus infection of the throat, which is capable also of producing rheumatic fever and rheumatic heart disease. There are likewise obvious metabolic disorders such as liver disease and jaundice which are capable

of producing profound damage to the lenticular nucleus, both in the postnatal period (kernicterus, in which damage of the basal ganglia occurs) and in later adult life. The association between liver disease and the lenticular nucleus is seen in cases in which there is a development of profound dystonia, athetosis and complex deformities characteristic of Wilson's disease. In this case it is now believed that a disturbance in copper metabolism is at fault. There also occurs classical damage to the lenticular nuclei, in such poisons as manganese and lead. One also sees structural alterations in cases of cerebral anoxia, carbon monoxide poisoning, and nitrous oxide anoxia in which profound changes are known to occur.

In addition to these situations one recognizes also the influence of trauma on certain cases. Although many alleged examples of traumatic Parkinsonism are open to considerable criticism, there seems to be occasionally bona fide cases in which patients do develop this syndrome as a result of cranio-cerebral injury. Moreover, one finds at autopsy hemorrhages and other changes purely traumatic in these structures, which could well explain this subsequent clinical picture.

In addition, the possibility of either embolism or ischemia from arteriosclerosis exists, as seen in patients with these lesions in arteriosclerosis.

The question must arise, therefore, which of these various possible pathogenetic factors is actually responsible for the development of these clinical pictures in cerebral palsy. This will be considered in the next section.

PATHOGENESIS OF CHOREO-ATHETOSIS IN CEREBRAL PALSY

There are two main theories for the causation of choreo-athetosis in cerebral palsy. This applies, of course, to those cases in which the etiology is not clearly established, including those presumed to date from early birth. It is recognized that there are many possible noxious conditions which can damage the corpus striatum and allied structures. One of these is kernicterus associated with jaundice at birth and usually due to Rh incompatability. In these cases, however, the history of jaundice following delivery with a resultant characteristic clinical picture makes the diagnosis fairly clear. We are speaking here instead of those cases in which the syndrome develops more or less quietly following birth or follows what is

comprehensively designated as "birth injury", which usually includes paranatal anoxia.

The first theory is that damage to the basal ganglia results primarily from the mechanical effects of dystocia. Deformation of the infant skull in delivery is believed to cause congestion, rupture, or occlusion of the internal cerebral veins (venous system of Galen). With a backing up of the blood in this system it is assumed that actual lesions occur in the form of focal hemorrhages or at least that there is a severe degree of congestion with consequent disturbance of the circulation in this area. It is likewise concluded that the resulting damage is responsible for alterations in the basal ganglia to a degree capable of symptom production.

The history of this theory dates back to a concept introduced by Schwartz,[1] who developed this concept on the basis of experimental evidence of birth injury. He believed that there was a suction effect on the head of the infant as it was delivered. Schwartz[2] has gone on record in a series of studies to the effect that changes in the white matter and basal ganglia of the fetal brain occur as a consequence of difficult birth. This theory has been accepted by a number of other writers, particularly in Germany, who have concluded that this is the correct explanation of these changes. This has also been elaborated by other writers in this country, including Marburg[3] and Malamud.[4]

I have made an effort to evaluate this problem, first by studying what is known about the effects produced by thrombosis of the internal venous system as found in the brain from other causes, (Ehlers and Courville).[5] These changes are indicated by an investigation of the area drained by the vein of Galen. The accompanying drawing implies the area of drainage, the right vein, and on the left side the actual distribution of the individual veins is shown (fig. 7). It should be noted that the regional white matter as well as the basal ganglia are included in this area.

In other words, any serious obstruction to this venous system will alter by focal hemorrhages both the white matter and gray matter of the region. Actual thrombosis of the veins, for some reason or another, tends to result in an asymmetry of the distribution of these lesions. This would indicate that, if the Schwartz theory were true, the lesions resulting therefrom need not be bilateral. Moreover, it is evident that these lesions will likely affect the white matter as well as the gray. One also finds frequently an associated throm-

bosis of the superior longitudinal sinus. In these instances changes in the cortex of the upper part of the cerebral hemispheres as well as in the subcortical white matter are to be found. Hemorrhages resulting from occlusions of the venous system occur in the various portions of the thalamus including its central part, portions of the lenticular nucleus, and the intervening limb of the internal capsule. The accompanying composite picture shows diagrammatically the distribution of the lesions found in cases I have studied (fig. 8).

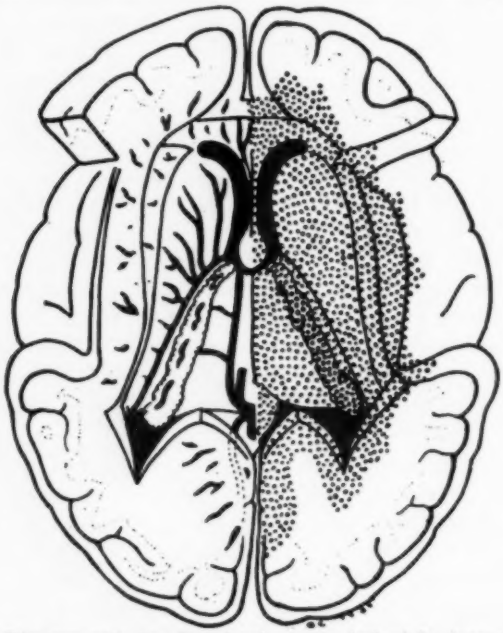

Fig. 7. Diagrammatic drawing showing area drained by internal venous system of Galen (left half) and actual distribution of vessels of system (right half).

A study of these lesions reveals that their locations following occlusion of the system are somewhat different from those of the lesions found in cerebral palsy. In the first place, the frequent involvement of the adjacent white matter would tend to exclude the lesions observed in general palsy. As a rule these variations in structure of the corpus striatum and allied gray matter are quite sharply limited to the gray matter itself. Moreover, the locations of gross hemorrhages with irregular involvement of the basal ganglia or white matter are entirely different from what one would

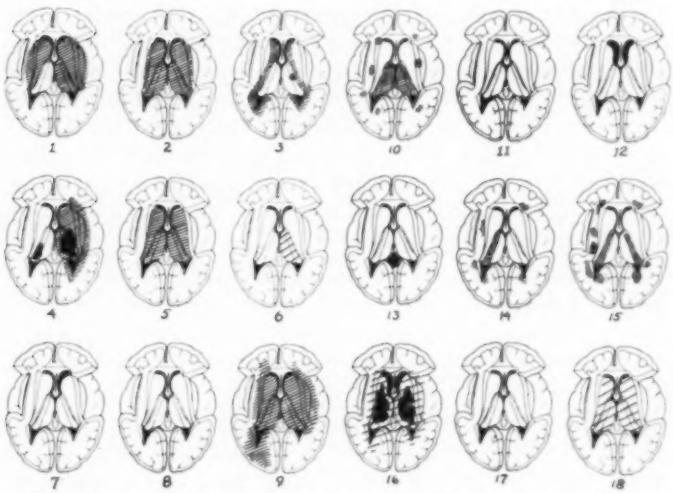

Fig. 8. Cerebral lesions found in a series of 18 cases of thrombosis of internal venous system of Galen verified at autopsy. The irregular bilaterality of the lesions, the pattern of ganglionic involvement and irregular involvement of regional white matter stand out in contrast to the lesions of status marmoratus and dysmyelinisatus. Larger areas covered by diagonal lines indicate red softening, smaller areas indicate collections of petchial hemorrhage and large solid black spots indicate gross hemorrhage.

anticipate on the basis of thrombosis. In addition, predominate alteration of the medial rather than the lateral aspect of the thalamus would tend to exclude vascular lesions as a hemorrhage. Therefore, occlusion of this internal system of veins is not likely to produce any of the ganglionic lesions found in cerebral palsy, such as have been described in the previous section. All of these lesions, it will be recalled, are rather sharply confined to the individual gray matter. This elaboration of the argument against the theory has been described in two papers already published Ehlers and Courville[5] and Courville.[6]

We need, therefore, to consider the second theory of ganglionic damage in cerebral palsy, that of paranatal anoxia. It should be recalled that either the corpus striatum on one hand, which is a combination of the caudate nucleus and the putamen, or the globus pallidus on the other, constitutes the central or "hub" lesion of the brain frequently produced in all types of cerebral anoxia. This is true even in cerebral anoxia resulting from cardiac standstill under spinal anesthesia. While cortical softening is also present, the con-

spicuous lesion is found in the globus pallidus. This of course is also true of the changes observed in carbon monoxide poisoning. Whether the brain is cut horizontally or vertically there are usually found small foci of softening in the globus pallidus. This nuclear mass tends to break down progressively and leave a sharply outlined cystic cavity which is almost the exact counterpart of the lesions found in one of our cases of cerebral palsy (see fig. 3). A similar lesion is found in cases of cerebral anoxia resulting from nitrous oxide anesthesia.

Perhaps there is no better illustration of the effects on the corpus striatum than that found in hyperinsulinism, in which the caudate nucleus and putamen seem to be selectively involved in the softening process. This is seen in cases reported under other circumstances, Courville.[8,9]

Perhaps a more precisely comparable lesion is that known as status dysmyelinisatus with changes found in fatal cases of cerebral anoxia from various causes. The loss of the myelin sheaths from the external capsule and the putamen produces practically the exact counterpart of the lesion found in status dysmyelinisatus, one form of ganglionic lesion in cerebral palsy (see fig. 6).

This leaves for final consideration the lesion known as status marmoratus or "marble state." Here the small, sharply circumscribed bundles of hypertrophic myelinated nerve fibers make a characteristic picture. These bundles are found occupying the lateral aspect of the thalamus, the lateral aspect of the putamen, and the caudate nucleus. Frequently these hypertrophic bundles are associated with similar changes in the overlying cortex, presenting a pathological picture of nodular cortical atrophy.

It has been shown, Courville[10] that nodular cortical atrophy is a result of an ischemic process of the cortical arteries which seems to be superimposed upon an anoxic state incident to paranatal asphyxia. The fact that this condition is found in conjunction with a similar finding in the basal ganglia suggests a common etiological factor. Malamud[11] noted that in 12 of 14 cases, status marmoratus occurred in patients who had had a clear history of "birth injury." Since the term "birth injury" is so poorly defined by many writers, there is very little reason to doubt that the so-called birth injury was in fact a paranatal anoxia insofar as the production of brain damage was concerned. Other observers, i.e. Benda[12] have come to similar conclusions in regard to clinical cases presenting the typical choreo-athetoid syndrome in cerebral palsy.

We are not yet fully informed as to the mechanism of production of status marmoratus although a similar experimental lesion was reported by Morrison.[13] He resected the cortex over the basal ganglia in developing animals and ultimately described changes that were at least reminiscent of those in status marmoratus.

The weight of evidence would therefore favor an anoxic etiology for these patients with damage to the corpus striatum and allied structures. There is no present satisfactory explanation for the mechanism of this lesion on any possible etiological basis. From a statistical cause, paranatal anoxia is a much more likely cause than is a circulatory disturbance incident to occlusion of the internal system of Galen.

SUMMARY

In this preliminary study of a somewhat neglected problem, one becomes aware of two situations regarding choreo-athetosis as seen in cerebral palsy. In one group of cases, the clinical picture of these hyperkinetic phenomena is so characteristic as to constitute the essential if not the only feature of the disease. It is this group which constitutes the so-called choreo-athetotic type of cerebral palsy. There is a second group of cases in which tremor, rigidity, and athetoid movements form only a part of the syndrome, the motor or cerebellar signs tending to obscure the hyperkinetic manifestations.

When one makes a study of the various possible lesions found in autopsied cases of cerebral palsy he is impressed with several basic facts. First, lesions limited to the basal ganglia and forming the conspicuous feature of the pathologic state may be found in patients who present the classical syndrome of choreo-athetosis. However, the location and degree of these lesions vary considerably in such cases. One also finds classical pictures of choreo-athetosis in persons who present no gross lesions of these structures. Conversely, physical changes in the basal ganglia which, during life, presented no significant manifestation may be found. One is therefore left with the conclusion that at times these abnormal movements are the result of cellular rather than structural damage in these cases. It is important, therefore, that we do not confuse the clinical picture of choreo-athetosis with any great degree of physical damage or a specific lesion in this system. That such manifestations are not infrequently found in cerebral palsy, however, demands a more critical study of the problem. On investigation of those instances in which the etiological factor is not clearly defined (as in cases

of cryptic paranatal anoxia, for example), one is faced with two current theories as to the cause of the manifestation. The currently most popular theory is that these lesions result from occlusion, either transitory or permanent, of the internal venous system of Galen. The arguments against this theory have been reviewed and pointed out in this study.

On the other hand is the likelihood that most of these lesions in the so-called "idiopathic" examples of extrapyramidal phenomena in cerebral palsy suggest paranatal anoxia as the essential cause. The arguments in favor of this conclusion are also pointed out in this contribution.

It is clear that more study is needed to evaluate fully the possibilities in this type of cerebral palsy.

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Hypertrophic Pyloric Stenosis of Infancy Associated with Ulcer . . .

A CASE REPORT

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HYPERTROPHIC pyloric stenosis of infancy is prone to occur in first born male children. It may also recur in the same family.[1] The stenosis is due to hypertrophy of the circular smooth muscle fibers of the pyloric canal. The cause of the hypertrophy is unknown but central nervous system damage, local neurologic imbalance, preexisting pyloric spasm and adrenal cortical insufficiency have all been considered as etiologies. It is thought by many to be congenital and pyloric muscular tumors have been reported in stillborn infants[2] and in a seven month fetus.[3] This may conflict with Wallgren's[4] work. He showed that the pyloric canal is normal roentgenographically during the first week of life in infants who later develop pyloric stenosis. One must consider, however, that there may be lesser degrees of pyloric stenosis without radiologic findings.

Assuming a preexisting narrowed pyloric canal in infants, whatever the etiology, it is thought that the mucosa is initially normal, becoming edematous as the curds are forced through the pylorus during feeding and resulting in thickening of the mucosa and hence gastric outlet obstruction. This is the sequence given to explain why the infants do not usually manifest symptoms of the condition until two to four weeks of age.

Hypertrophic pyloric stenosis in older children and adults is most often associated with peptic ulcer.[5,6] Hypertrophic pyloric stenosis of infancy, however, is not usually associated with ulcer disease.[7] Singleton, on the other hand, says that "perhaps superficial ulceration and mucosal edema in the region of the pyloric canal with partial obstruction of the gastric outlet or reflex vagal stimulation is responsible for the majority of cases of hypertrophic pyloric stenosis even in young infants."

The following case report illustrates hypertrophic pyloric stenosis of infancy associated with a peptic ulcer.

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This six week old Puerto Rican male was hospitalized 11/16/60 with the chief complaint of intermittent vomiting since shortly after birth. The vomiting was non-projectile and occurred approximately 30 minutes after feedings. The child was "always hungry." The vomitus was not bile-stained. The child weighed 6 pounds 12 ounces at birth and 5 pounds 8 ounces on admission.

Figs. 1 & 2. Arrows on fluorographic spot films indicate ulcer niche at proximal end of stenotic pylorus.

On examination the child was noted to be moderately dehydrated. The abdomen was soft and a 2 cm mass was palpable in the right upper abdominal quadrant.

Plain film of the abdomen was not remarkable. When the stomach was examined fluoroscopically, hypertrophic pyloric stenosis was thought to be present. The fluoroscopic spot films showed a niche in the proximal pyloric canal which was interpreted as an ulcer. (Figs. 1 & 2)

An attempt was made to hydrate the patient prior to surgery but he expired suddenly on 11/20/60.

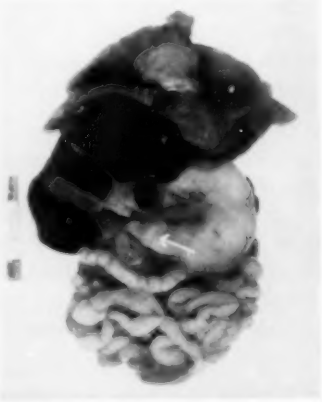

Fig. 3. The arrow is directed to the hypertrophic pyloric stenosis in the gross autopsy specimen.

Autopsy showed hypertrophic pyloric stenosis (Fig. 3) with a small, superficial ulcer at the proximal end of the stenotic pylorus. (Fig. 4)

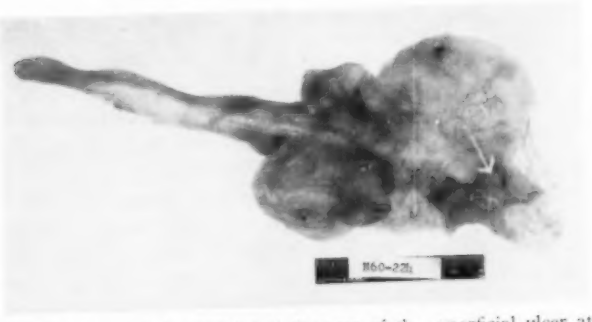

Fig. 4. The stomach is opened and the area of the superficial ulcer at the proximal end of the stenotic pylorus is indicated by the arrow.

CONCLUSION

An autopsy proven case is presented of hypertrophic pyloric stenosis of infancy associated with a peptic ulcer. This association is usually present in older children and adults and is rare in infants. No conclusion as to cause and effect is drawn.

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Hydroxyzine in the Treatment of Rheumatic Chorea in Children

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Our knowledge of the nature of the nervous disturbance in chorea depends more on physiological studies than on pathological findings. The latter have shown diffuse changes in the brain including corpus striatum, basal ganglia and cortex. On the other hand, physiological studies suggest that the abnormal movements of chorea arise from the disorganization of a circular pathway passing through the caudate nucleus and putamen, globus pallidus, ansa lenticularis, Forel's fields, ventro-lateral nucleus of the thalamus, and thence to the precentral cortex.[1] Psychological factors are stated to play a role—predisposing or aggravating—in chorea, the subject of which shows emotional instability. Hence the rationale, based on both physiological and clinical considerations, for the use of sedatives in chorea. With the advent of tranquillizers, chorea seemed to be one of their fields of trial. Hereby we report on the use of one of them, hydroxyzine, for the first time by us, in this disorder.

MATERIAL AND METHODS

Most cases diagnosed as Syndenham's chorea were treated as in-patients. Before treatment, they were observed for 2 to 3 days to assess the severity of the disorder. Amongst other tests, the average time taken to perform a given movement, and the degree of coordination with which it is done were recorded before, and twice weekly during treatment. No case was considered cured until the defects in power and tone—best demonstrated by the posture of the outstretched hands and the hand grip—have disappeared, and the patient can do complex movements without incoordination. The patient's weight, blood pressure, and blood picture and sedimentation rate were estimated before and during treatment.

Drug treatment for the 'trial cases' consisted of hydroxyzine (Atarax) in doses of 50 mg. t.i.d.

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TABLE I.

CLINICAL DATA AND SYMPTOMS OF ALL TREATED CASES

	Trial Cases	*Controls*
Total number of cases	12	10
Cases with emotional disturbances	10	8
" " chorea mollis	0	1
" " clinical signs of rheumatic activity	2	2
" " active endocarditis	0	1*
" " inactive "	1**	0
" " Hb 70% or less	9	7
" " E. S. R. 20 (Westergren)	3	6

* Mitral incompetence
** Mitral stenosis

However, no assessment of a new drug is complete until it has been concurrently compared with an old one. For this purpose other untreated cases of chorea were put on phenobarbitone 0.03 gm. b.i.d. for children aged 8 years or less, and 0.03 gm. t.i.d. for older children. Cases so treated will be referred to as 'controls'.

CLINICAL NOTES

In all there were 12 trial cases and 10 controls. Of the trial cases, two were mild, 9 moderate, and one severe (Table 2). The last had marked difficulty in swallowing and articulation, and an unsteady gait, in addition to wild abnormal movements and emotional upset. Conversely, in mild cases the abnormal movements were of a low rate and magnitude, incoordination was not gross, and the emotional disturbance not apparent. The average duration of the present disease in the trial cases before treatment was 17.1 days.

Three cases (No. 1, 9, 12) relapsed at intervals of 4-8 months after discharge and were re-admitted. They were included amongst the 10 controls'. Of the latter there were 2 mild, 7 moderate and one severe cases (Table 3). The average duration of the last attack of chorea before treatment was 15 days. The controls were thus comparable in their initial condition with the trial cases.

Other clinical data concerning the cases are shown in Tables 1-3. Mitral stenosis was present in one case, No. 7. Another case (No. 17) had a soft apical systolic murmur during its previous admission for chorea, that disappeared, to recur as a loud early pansystolic murmur propagated to the axilla (mitral incompetence) when seen again in relapse of chorea six months later.

Table 2 - Progress of hydroxyzine - treated cases of chorea

Serial No.	Hospital No.	Age Years	Sex	Severity	No. of attack	Durat. last one d.	Daily dose mg.	Time to def. impr. d.	Time to recovery d.	Remarks
1	955	11	F	Severe	3	60	150-225	22	40	dose increased to 225 on 11th d.c On R. for last 14 d.
2	962	9	F	mod.	1	9	150	11	20	
3	GA 71241	5.5	F	"	1	10	100	7	7	not followed up.
4	1015	7	F	"	1	5	150	4	23	
7	1028	10	F	"	3	30	150	14	-	further impr. on R. was of the same order
8	1039	9	M	"	1	10	150	4	17	
9	1087	5	F	mild	2	30	150	7	19	transient drowsiness early in tt.
10	1136	10	F	mod.	2	7	150	8	-	no further impr. on R. for 12 d.
11	1167	8	F	"	3	14	150	6	15	
12	91	9	F	"	2	1	150	5	18	
13	130	12	M	mild	2	5	150	4	15	
14	532	7	F	mod.	1	25	150-200	12	31	dose inc. to200mg.on9th d.

Abbreviations : d = day, def. = definite, impr. = improvement, R. = reserpine, mod. = moderate, tt = treatment.

RESULTS OF TREATMENT

All cases benefited from hydroxyzine, definite improvement occurring after 7 days or less in 7 out of 12 cases, and within 2 weeks in 11 cases (Table 2). Moreover, of 9 cases treated with hydroxyzine alone for at least 3 weeks, six recovered completely or almost so within 3 weeks. The dose of 150 mg. daily was effective in all but 2 cases (No. 1 and 14) in which it had to be increased to 200-225 mg. daily before the abnormal movements were controlled. A dose of 100 mg. daily was quite ineffective in case 3, aged 5.5 years; it subsequently responded rapidly to 150 mg. daily.

In 3 cases, after periods of 8, 14 and 26 days of treatment with hydroxyzine, it was replaced by Reserpine in 0.6 mg. daily dosage, so as to compare the effect of the 2 drugs in the same patient. None achieved a more rapid response on Reserpine, although the latter drug was used later in the course of chorea which is known to be naturally regressive; the institution of such therapy following a course of hydroxyzine would thus be rather at an advantage.

The first effect of hydroxyzine was on the emotional upset. Next followed the effect on the abnormal movements, and finally on coordination, power and tone.

The only side-effect noted was mild drowsiness, occurring early in treatment of one case (No. 9), to disappear later without reducing the dose of hydroxyzine. There were no changes in the pulse, blood pressure or blood picture.

Table 3 – Progress of phenobarbitone – treated cases of chorea

Serial No.	Hosp. No.	Age Years	Sex	Severity	No. of attacks	Durat. last one d.	Daily dose mg.	Time to def. impr. d.	Time to recovery d.	Remarks
15	558	12	M	mild	2	14	90	16	–	No recovery after 21 d.
16	631	10	F	mod.	3	45	90	30	45	
17	[illegible] 46736	5.5	F	mild	2	30	60	23	–	c/o sleepiness after phenobarb.
18	[illegible] 46801	9.5	F	mod.	3	7	90	10	–	No recovery after 30 d. Extreme drowsiness & ataxy after this dose of phenobarb.
19	709	6	F	mod.	1	6	60	17	31	marked drowsiness & ataxy during first 4 d. tt.
21	736	9	F	mod.	2	9	90	22	29	
22	843	8	F	Severe	1	5	90	25	–	No recovery after 34 d.
23	824	12	F	mod.	4	10	90	24	35	
24	942	9	M	mod.	3	15	90	–	–	No def. impr. after 24 d.
25	979	7	F	mod.	1	3	60	12		Not followed up.

The progress of the phenobarbital-treated cases is shown in Table 3. No case definitely improved within one week, and only one case did so within 2 weeks. Of 9 followed-up cases no recovery occurred in less than 3 weeks. Two cases (No. 18, 19) experienced marked drowsiness and ataxy, necessitating reduction of phenobarbital dosage in Case 18.

DISCUSSION

Hydroxyzine which is a diphenylmethane derivative belongs to the group of tranquillizers that are most effective in the neuroses and minor functional disturbances.[2] It has also been used in child psychiatry, with encouraging results in such conditions as behavior disorders, tics, repetitive motor disorders and night terrors.[3,4]

The tranquillizing effect of hydroxyzine is produced essentially by inhibition of the conditioned reflexes responsible for the conveyance of the emotional impulse, but it has no depressive effects on the cortical or subcortical functions.[5] This was shown by animal experiments in which the ataraxed animal was put under the effect of benzedrine.[5] Hence it is not a neuroleptic agent like chlorpromazine or reserpine, i.e. it acts without producing the usual effects of sedation or hypnosis, since it does not affect the sleep conters.[5,6] However, Schuller,[6] has shown that clinically it is unquestionable that a similar effect to the neuroleptic one of reserpine is obtained with large doses of hydroxyzine, and that psychotic processes are practically influenced only by very large doses, which were sometimes more than 500 mg. daily in adults. Similar relatively large doses for the age group of the present work were needed to control the abnormal movements and the incoordination of voluntary movements of chorea. Hence the mode of action of hydroxyzine in this disorder is most probably one of

sedation produced by unusually large doses of the drug. Such doses, however, were well tolerated, and the drug was practically free from side-effects. The latter were reported to occur rarely in adults. The commonest was drowsiness, but of only a brief duration, since the drug is rapidly absorbed and its effect comes to a maximum after 2 hours.[7]

In contrast, reserpine is slowly absorbed, and hence is liable to have a cumulative action. In general, its side-effects, notably drowsiness, hypotension, bradycardia and increase of secretions produced by its cholinergic effect, are not so rare. The work of Hanna et al.[8] suggests a more rapid response to doses of reserpine similar to those we used in 3 cases previously treated with hydroxyzine.

On the other hand, the results of this controlled trial have shown, for the first time, that the tranquillizer hydroxyzine is a more effective treatment of rheumatic chorea than phenobarbitone hitherto considered to be "perhaps the most effective"[9] drug for this condition. Furthermore, the side-effects were more marked with phenobarbitone than with hydroxyzine during this work. This, however, may be a coincidence, for it is rare for the former drug to produce such marked drowsiness and ataxia in the dosage used, unless in case of hypersensitivity to it.

SUMMARY

Twelve children suffering from rheumatic chorea were treated with hydroxyzine, and its effect compared with that of phenobarbitone used in 10 other cases of comparable initial severity. In three cases after an initial treatment with hydroxyzine, a trial of reserpine followed. Hydroxyzine was shown to be more effective than phenobarbitone both in control of the abnormal movements and in the immediate cure of the disease, not to speak of relapses which were not expected to be influenced by any previous therapy. However, to be effective, hydroxyzine had to be used in daily doses of 150 mg. or more. Such dosage was safe, no serious side-effects ensuing. The mode of action of the drug is discussed. Reserpine does not seem to offer more advantages.

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Treatment of Non-Suppurative Myringitis and Otitis Media

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THE change in the pattern of the total spectrum of infections since the advent and increasing use of more and more efficient antibacterial agents, has become evident to clinical practitioners within the past decade. Along with greater knowledge, definition and classification of viral diseases, has come a realization of the startling increase in the proportion of infections for which viruses are responsible. As our experience with viral diseases has grown, so also has our ability to make specific clinical diagnoses of these disorders.

Myringitis and non-suppurative otitis media has been noted to have a high incidence in a variety of viral disorders by numerous observers.[1,2,3,4] Although these conditions are not responsive to antibiotics, they continue to be treated in a similar manner to acute purulent otitis media in the large majority of cases. The general attitude of acceptance of the use of antibiotics especially in respiratory infections, even where not specifically indicated, has been one factor promoting this state of affairs. Also, the acuteness of the symptoms, the distress and pain of the patient, usually a young child and consequent parental pressure, has a tendency to promote the use of, most frequently, the penicillin injection, or else, high dosage oral broad spectrum antibiotics.

It has been our feeling that this blanket type of therapy without efforts by pediatricians and others examining these patients to make a more specific clinical diagnosis is reprehensible on theoretic grounds. Furthermore, there is considerable evidence that this type of antibiotic therapy where it is not indicated, may promote serious sequellae. Freeman and Freeman,[5] Theobald,[6] Updigraff,[7] Woodward,[8] and Samuels,[9] have mentioned some of these which range from simple serous otitis to adhesions, cholesteatoma and deafness. Freeman and Freeman state "While antibiotics and chemotherapeutic agents have reduced the incidence of purulent complications, their widespread use may be the cause of the augmented number of middle ear effusions now being seen." These investigators stress

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the importance of preventing accumulations of non-purulent fluid in the middle ear, or its removal if this accumulation has occurred.

Myringitis and otitis media are conditions deserving of careful and continued supervision and therapy. The one-visit, one-shot treatment may be effective in most cases, but certainly leaves the door open to development of serious, often irreversible, tragic sequellae in young children. It has been our practice whenever possible to follow cases of otitis media on a daily basis.[10] We have made every effort on the basis of general clinical evaluation as well as careful otologic scrutiny to make a specific clinical diagnosis of the otitis or myringitis. It has been our practice to withhold antibiotics at the onset in those conditions where the appearance of the drum membrane was specific, as in bullous myringitis, or the general clinical diagnosis was of a viral disease, such as measles, influenza, ECHO virus, etc. In these conditions, antibiotics are not indicated unless purulent complications supervene, and this most frequently occurs on the second, third or fourth day. With daily observation, the time to begin antibiotics if complications occur should be readily evident. Normally these viral infections show a regular pattern of resolution beginning after 24-48 hours. Any continuance of symptomatology or lack of resolution after this period warrants the initiation of chemotherapy or antibiotics in good dosage. In those cases where this can be avoided, and these are in the majority, the hazards of serous accumulations, adhesions, and possible deafness have been minimized.

During the acute stages, it is necessary only to treat the pain and congestion. Heat, analgesics and local instillations into the ear canal are the modalities to be used. The ear instillations should be anticongestive and dehydrating in nature, since the diminution of serous exudate is of prime importance. The following group of cases were collected to illustrate these principles of therapy.

METHODS

A group of forty-four children with a non-suppurative type of myringitis or otitis media was assembled over a period of time. Criteria for making the diagnosis were both clinical and laboratory. All children presenting themselves with ear complaints were given a complete physical and otologic examination, and blood counts and urinalyses were performed. In an effort to make our test group as specific as possible, all doubtful cases were excluded from the study. Reasons for exclusion from the study group were:

1. Evidence of associated infection in the nasopharynx which could possibly have an active bacterial component, e.g., cases with exudation or lymphodenopathy. 2. Evidence of suppurative infection in any other area. 3. Elevation of white blood count and/or shift to the left. 4. Bulging drum.

Our group therefore was composed of children with catarrhal or bullous myringitis, with or without some evidence of fluid, but without loss of landmarks, with low or normal blood counts and without other evidence of possible bacterial infection elsewhere in the body.

The group consisted of male and female children from one to nine years and, as shall be further detailed, ranging from simple catarrhal myringitis to influenza, measles, and ECHO virus infections with otitis.

They were divided into two groups, completely at random, assigning them alternately as they presented themselves without regard to age, or severity of the disorder, as long as the patient satisfied our criteria for the non-suppurative type of infection. All children were examined daily for five days. The first group was treated entirely symptomatically with heat locally applied in the form of a heating pad or hot water bag and the instillation of a non-irritating dessicant and decongestant consisting basically of a highly purified glycerol with small quantities of antipyrine and benzocaine added.* Where pain was severe, aspirin was administered at four-hour intervals until pain subsided.

The second group was treated with local heat, aspirin where necessary and tetracycline in the dosage of 30 mgms per kilogram, divided into four, six-hour doses.

RESULTS

The results are most simply presented in Table 1.

CONCLUSIONS

1. The average period of time taken for the subsidence of symptoms was significantly shorter in Group 1 (Symptomatic Treatment) than in Group 2. (Antibiotic Therapy).

2. The average time for a cure, that is disappearance of all symp-

* Auralgan: Supplied by Dobo Chemical Co., New York City.

TABLE 1

Group 1
(no antibiotics)
Results

Pt.	Name	Race	Sex	Age	Diagnosis	Symptoms	Final Results
1.	L. W.	W.	F.	3	Bullous Myringitis	Subsided 1 day	Cured 3 days
2.	S. R.	W.	F.	3	ECHO Virus Catarrhal O. M.	Subsided 12 hrs	Cured 3 days
3.	Z. G.	W.	M.	7	Hemorrhagic O. M.	Subsided 12 hrs	Cured 4 days
4.	D. M.	W.	M.	8	Catarrhal O. M.	Subsided 1 day	Cured 4 days
5.	D. R.	W.	M.	4	ECHO Virus with Catarrhal O. M.	Subsided 8 hrs	Cured 2 days
6.	O. T.	C.	F.	3	Catarrhal O. M.	Continued 2 days	Antibiotic Cured 5 days
7.	J. F.	W.	M.	8	Grippe with Catarrhal O. M.	Subsided 1 day	Cured 3 days
8.	A. V.	C.	M.	4	Adenovirus with Catarrhal O. M.	Subsided 12 hrs	Cured 3 days
9.	W. W.	C.	F.	2½	Pharyngitis Catarrhal O. M.	Subsided 8 hrs	Drained spont. 2nd day
10.	H. B.	W.	M.	10	Catarrhal O. M.	Subsided 8 hrs	Cured 2 days
11.	G. P.	W.	M.	5	Allergic Rhinitis with Catarrhal O. M.	Subsided 1 day	Cured 3 days

Group 2
(antibiotics)
Results

Pt.	Name	Race	Sex	Age	Diagnosis	Symptoms	Final Results
1.	P. Z.	W.	M.	4	Catarrhal O. M.	Subsided 1 day	Cured 3 days
2.	S. R.	W.	M.	5	Catarrhal O. M.	Subsided 1½ days	Cured 3 days
3.	F. C.	W.	F.	6	Influenza with Catarrhal O. M.	Subsided 1 day	Cured 3 days
4.	H. G.	C.	M.	4	Measles with Hemorrhagic O. M.	Subsided 2 days	Cured 4 days
5.	R. I.	W.	F.	7	Catarrhal O. M.	Subsided 1 day	Cured 3 days
6.	A. D.	W.	M.	6	Catarrhal O. M.	Subsided 1½ days	Cured 3 days
7.	C. F.	C.	F.	5	Influenza with Bullous Myringitis	Subsided 2 days	Cured 4 days
8.	R. T.	W.	F.	11	O. M.	Subsided 1 day	Cured 3 days
9.	M. G.	W.	M.	5	O. M.	Subsided 1½ days	Cured 3 days
10.	C. M.	C.	F.	2	Measles Catarrhal O. M.	Subsided 2 days	Cured 4 days
11.	J. J.	C.	M.	3	Measles with Catarrhal O. M.	Subsided 3 days	Cured 5 days

12.	W. G.	C.	M.	7	Grippe with Catarrhal O. M.	Subsided 8 hrs	Cured 2 days
13.	S. R.	W.	F.	3	ECHO Virus Catarrhal O. M.	Subsided 12 hrs	Cured 3 days
14.	J. S.	W.	M.	4	Rose fever with Catarrhal O. M.	Subsided 1 day	Cured 4 days
15.	T. G.	C.	M.	2	Bullous Myringitis	Subsided 1 day	Cured 3 days
16.	J. B.	C.	M.	2½	Grippe with Catarrhal O. M.	Subsided 4 hrs	Cured 2 days
17.	M. H.	W.	M.	4	Measles with Catarrhal O. M.	Subsided 8 hrs	Cured 3 days
18.	J. C.	W.	M.	1½	Adeno-virus with Catarrhal O. M.	Subsided 8 hrs	Cured 2 days
19.	N. T.	C.	M.	5	Catarrhal O. M.	Subsided 8 hrs	Cured 1 day
20.	S. P.	W.	F.	9	Rose fever with Catarrhal O. M.	Subsided 12 hrs	Cured 2 days
21.	R. S.	W.	F.	8	Pharyngitis with Cat. O. M.	Subsided 8 hrs	Cured 3 days
22.	D. G.	C.	M.	3½	Measles with Hemorr-hagic O. M.	Subsided 1 day	Cured 4 days

12.	J. S.	W.	F.	2	Catarrhal O. M.	Subsided 1 day	Cured 3 days
13.	R. R.	C.	F.	1½	Pharyn-gitis with Catarrhal O. M.	Subsided 1 day	Drained spont. 3rd day
14.	B. S.	W.	M.	6	Pharyn-gitis with Catarrhal O. M.	Subsided 1 day	Cured 3 days
15.	H. G.	C.	F.	3	Catarrhal O. M.	Subsided 1 day	Cured 3 days
16.	S. B.	C.	M.	4	Grippe with Catarrhal O. M.	Subsided 1 day	Cured 2 days
17.	S. H.	W.	M.	6	Measles with Catarrhal O. M.	Subsided 1 day	Cured 3 days
18.	M. C.	C.	V.	4	Adeno-virus Catarrhal O. M.	Subsided 1 day	Cured 3 days
19.	L. P.	W.	F.	2½	ECHO virus with Catarrhal O. M.	Subsided 12 hrs	Cured 3 days
20.	N. T.	C.	M.	5	Catarrhal O. M.	Subsided 1 day	Cured 2 days
21.	E. S.	W.	F.	8	Pharyngitis with Catarrhal O. M.	Subsided 1 day	Cured 3 days
22.	S. P.	W.	M.	1½	Catarrhal O. M.	Subsided 12 hrs	Drained spont. 2nd day

Explanation: Symbols O. M.—Otitis Media
Cat—Catarrhal
Subsided—refers to the time that complaints of pain or discomfort ended
Cured—refers to the time when all evidence of active inflammatory process has disappeared in direct visualization of the tympanic membrane

toms of active inflammation, was approximately the same in both groups.

3. One case, number 6 (O.M.) of Group 1, developed purulent otitis media on the third day, which responded to tetracycline 30 mgms/kg in three days.

4. Three cases, number 9, W.W. of Group 1 and numbers 13 R.R. and 22 S.P. of Group 2, developed spontaneous drainage of thin serous material. All three cases were in the very young age group where this might be expected. Antibiotics in substantial dosage had no effect on prevention of this phenomenon.

5. In four instances, siblings became spontaneously ill. These were numbers 15, 17, 18 and 21. The last were twin girls. In all of these cases, where controlled comparisons were better because of the sibling situation, the group treated with ear instillations had more rapid subsidence of symptoms than the second group and the time for cure was approximately the same.

6. Case 19 in Group 1 and case 20 of Group 2 are the same child. This boy developed a second catarrhal otitis media in the opposite ear about a week after subsidence of his initial infection. We took the opportunity to use him as his own control. He also, experienced more rapid relief of symptoms with ear instillations than with antibiotics.

DISCUSSION

Ideally, otitis media should be followed with daily examinations. Under these conditions, viral myringitis and otitis media may be readily diagnosed and antibiotics withheld until the appearance of a suppurative complication (which is uncommon) indicates their usage. This type of medical management could do much to minimize the development of serous otitis which could lead to adhesions and, if untreated, to deafness. While we got no serous accumulations in the twenty-two cases in our study who were given antibiotics and the incidence in general is not high, the occurrence in a small, but substantial percentage of cases is well documented.[5,6,7,8,9]

In the comparative study reported above, a conservative regime, utilizing a decongestant dessicant local instillation into the ear had considerably better success in controlling the symptoms of the disorder, which are most distressing, and there was no significant difference in the percentage or time or ultimate cure of the infection.

The one instance where a purulent complication occurred deserves some discussion. Under the ideal type of regimen, that is,

daily observation of the patient with otitis media or myringitis, there would seem to be no reason why antibiotics could not be withheld until indications appear for their use. Where this type of close supervision is not possible, it may be necessary to utilize antibiotics in prophylactic dosage to prevent this complication. However it should be clearly understood that these antibiotics have no effect upon the course of the initial disease, and they should be used in small dosage only.

SUMMARY

1. The indiscriminate use of large antibiotic dosage in non-suppurative ear involvement has been suggested as a possible predisposing cause of serous otitis and ensuing serious ear disorders.

2. In a comparative study of forty-four myringitis or otitis media cases, a conservative regime using instillations of dessicant-decongestant gave considerably quicker relief of symptoms and at least equivalent cure rates and speeds as a group receiving antibiotics.

3. Ideally, cases of otitis media and myringitis of non-suppurative nature should be examined daily and antibiotic therapy withheld until there is a specific indication for it. Where this regimen is not possible, antibiotics in small prophylactic dosage may be indicated in conjunction with the use of local instillations as used above, for relief of pain and other distressing symptoms.

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Activities of The Poison Control Center . . .

ETHYLENE DICHLORIDE POISONING

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CASE 1

THIS case was reported from Mid Island Hospital, Bethpage, Long Island. The patient, a 22-month old white male, found some glue which was lying around the home. He walked into the kitchen and his mother smelled the glue on his breath. She called the New York City Poison Control Center and was informed that the glue contained ethylene dichloride (toxicity similar to carbon tetrachloride). Shortly thereafter, the infant began vomiting and retching. He became somewhat cyanotic and the mother brought him to the Emergency Room at Mid Island Hospital. He had a convulsion there, was seen by a resident physician and lavaged.

The reporting physician stated that when he saw the patient (approximately 15 minutes after the patient was treated in the emergency room) the infant seemed alert and well and the vital signs were normal. He was admitted for observation. Retching continued for approximately another two hours but, thereafter, he began taking milk and fluids without difficulty. He urinated 3 to 4 times during the afternoon, his vital signs were normal and he seemed well. At approximately 8 P. M., 12 hours following inges-

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tion, his respirations increased, he became more and more cyanotic, suddenly went into complete cardiovascular collapse, and died despite supportive measures. At postmortem the Medical Examiner reported that all organs reeked of glue—liver, kidneys, stomach (gastritis) and brain. There was also a moderate cerebral edema.

The autopsy was performed by Dr. H. H. Abrahams, Deputy Medical Examiner, and the findings were as follows:

External Examination: The body was that of a 1 year, 10 month-old white male child, measuring 2 feet, 7 inches in length, and weighing approximately 35 pounds. The hair was light blonde; the eyes blue. The lips and face were cyanotic. No odor could be detected from the mouth. The teeth had erupted. There was no abnormal motility of the neck. The chest was symmetrical. The abdomen was not distended. The extremities were cold and rigid. There was considerable diaper dermatitis around the scrotum and the buttocks.

Incision: On incision, the subcutaneous fat was about 1/8 of an inch in thickness. The muscular layer was moderately well developed. There was no free fluid in the peritoneal cavity. The liver was at the costal margin. The right leaf of the diaphragm extended to the fifth rib; the left leaf to the fifth interspace. The pleural spaces were free of fluid and adhesions. There was marked congestion of the lungs. The pericardial sac contained about 2 cc. of clear fluid.

Heart: The heart weighed 25 grams. It had a dark brown color. The right auricle was not increased in size. The tricuspid valve leaflets were thin and delicate. The right ventricle was neither hypertrophied nor dilated. The intraventricular septum was intact. The pulmonary valve leaflets were natural; the pulmonary artery free of clots. The left auricle was not enlarged. The mitral valve leaflets were thin and delicate. The left ventricle was neither hypertrophied nor dilated. The aortic valve leaflets were natural. The coronary ostia were patent. The coronary vessels were thin-walled and elastic. The myocardium of the left ventricle was firm in consistency and had a dark reddish-blue congested appearance.

Lungs: The right lung weighed 50 grams, and had a strong aromatic odor similar to the stomach contents. The bronchi contained a small amount of whitish fluid. On section of the lung, the cut surface had a reddish-blue appearance. In the more peri-

pheral portions of the lower lobe, it had a congested reddish-blue appearance. This congested portion of the lung involved approximately 20% of the lower lobe. The left lung weighed 40 grams and grossly resembled the right, including the peripheral areas of congestion of the lower lobe.

Liver: The liver weighed 400 grams. It had a dark reddish-brown appearance. The surface was smooth. On section of the cut surface, it had a finely lobulated congested reddish-brown appearance. The gall bladder was thin-walled and contained about 3 cc. of greenish-brown bile. The biliary ducts were patent. The liver had a strong aromatic odor.

Genito-Urinary System: The right kidney weighed 15 grams. The capsule stripped with ease revealing a smooth congested reddish-brown cortical surface. The cortex measured about 2-3 mm. in thickness. On section, the cut surface had a congested reddish-blue appearance involving both cortex and medulla. The pelvis and ureter were not dilated. The left kidney weighed 15 grams and grossly resembled the right. Both had a strong aromatic odor. The bladder contained approximately 10 cc. of turbid yellow urine with a very strong aromatic odor. The genitalia were normal puerile male.

Gastrointestinal Tract: The mucosa of the esophagus was mildy congested. The stomach contained about 40 cc. of whitish turbid fluid with whitish particulate matter in it, having a very strong obnoxious aromatic odor. The gastric mucosa was markedly congested having a fiery red color. The color changes ended abruptly at the pylorus. The lining of the duodenum appeared normal. The gastric contents were saved for toxicological study, as well as the contents of the small bowel, separately from the contents of the large bowel. There was no congestion of the small or large bowel.

Pancreas and Adrenals: Normal.

Head: The cerebral-spinal fluid was clear. The brain weighed 1200 grams and showed marked acute edema with flattening of the sulci and gyri. The cerebral vessels were also markedly congested and there was no evidence of intracerebral hemorrhage or tumor. The brain had a strong aromatic odor.

Anatomical Summary: Gastrointestinal Tract: Gastric contents had a very strong aromatic odor and there was marked acute gastric congestion.

Genito-Urinary System: Acute congestion of kidneys with strong aromatic odor of kidneys and urine; diaper dermatitis to scrotum and buttocks. Head: Marked acute congestion and edema; aromatic odor to brain. Lungs: Marked peripheral congestion; aromatic odor. Liver: Acute congestion; strong aromatic odor. Heart: Acute congestion.

Toxicologic Examination: Ethylene dichloride present in trace amounts in lungs, stomach contents and brain.

Microscopic Examination: Stomach: Acute hemorrhagic congestion of mucosa. Lungs: Focal acute hemorrhagic congestion. Brain: Acute congestion. Liver: Cloudy swelling. Kidney: Cloudy swelling. Heart: Acute congestion.

Final Diagnosis: Acute ethylene dichloride intoxication, accidental.

CASE 2

Another case from the ingestion of a toy airplane glue was reported in a two-year old white male. While visiting with his mother the home of a friend who builds toy airplanes as a hobby and who purchased a one-gallon jug of glue for this purpose, the child found the container of glue and swallowed some of its contents. He immediately experienced some burning of the mouth and throat and was taken to a hospital several hours following ingestion because of recurrent vomiting.

On admission to the hospital the patient presented the following symptoms: dyspnea, vomiting and coma. The laboratory findings indicated an icterus index of 3; alkaline phosphatase 3.7; cephalin flocculation, negative; thymol turbidity 2.8; blood cholesterol 254; total proteins 7.1; and albumin globulin ratio 5.1/2.0. The patient was treated with oxygen, caffeine sodium benzoate, and lobeline, and after six days of hospitalization he made a complete recovery.

DISCUSSION

Ethylene dichloride is also known as 1, 2-dichlorethene and is used as a solvent and as an insecticide among other uses. It is reported to have a narcotic action similar to that of chloroform and carbon tetrachloride. Fatalities have occurred in adults from the ingestion of 30-70 grams. The lethal dose for children is naturally much lower. The symptoms may resemble those of carbon tetrachloride or chloroform poisoning.

As in this case, depending on the dosage and the amount of food in the stomach, hours may elapse before manifest symptoms appear. The most common symptoms are nausea and vomiting which, as in this case again, is usually recurrent and the vomitus may contain blood. The vomiting may be followed by diarrhea and is generally associated with abdominal pains of moderate or marked severity, trembling and weakness. This is followed by dizziness, drowsiness, headaches, stupor, dyspnea, coma and collapse which may terminate fatally. In severe cases in addition to vomiting, diarrhea, dyspnea and cyanosis, the pulse becomes shallow and rapid and the pupils become dilated or may fail to react altogether. There is a fall in the blood pressure and temperature; the patient usually goes into shock. The urine may contain albumin, sugar and casts because of kidney damage. Pulmonary edema and pneumonia may develop. Death is usually due either to respiratory or circulatory collapse.

On autopsy, as in the case reported, kidney and liver damage is found. The kidneys show extensive tubular necrosis with calcifications. There may also be fatty degeneration of the heart and the brain is hyperemic, showing signs of multiple hemorrhages.

In addition to ingestion, there have been reports of ethylene dichloride poisoning resulting from inhalation. In cases due to inhalation, corneal lesions have also been frequently reported. Such lesions have also been reported from subcutaneous ingestion of ethylene dichloride which would indicate that the corneal lesions are not necessarily merely a result of direct contact. It has been reported that the mortality rate and the incidence of fatty changes may be considerably reduced by the immediate administration of methionine, BAL, and cysteine. This is reported to be particularly helpful if given promptly after an ingestion. Immediate gastric lavage, high colonic irrigations, blood transfusions and intravenous therapy have been also recommended. Otherwise, the treatment is entirely supportive. The best treatment of course is total prevention.

Ethylene dichloride combined with carbon tetrachloride is a widely used insecticide-fumigant in the baking industry. The use of ethylene dichloride as a solvent component for hobby kits for use by children is strongly disapproved.

At the present time considerable excitement prevails especially among laymen about the misuse of plastic cements containing

solvents. It would appear that with each successive news report of incidents involving plastic cements that an increase in incidents occurs. The solvents most involved are trichloroethylene, toluene, cyclohexanol but may be any of a larger list of other available organic liquids. The practice of expelling the contents of the tube into a paper bag and inhaling the solvents has produced among the teenage users reports of euphoria, undue excitement, "jags," and even unconsciousness. In conjunction with the use of alcoholic beverages, the symptoms are aggravated. Although central nervous system, liver and kidney damage may ensue, thus far in the cases reported such documentation is still scanty. There is always a danger that one of the more hazardous solvents may be substituted.

Treatment: There is no specific antidote for ethylene dichloride poisoning. The best therapy is of course total prevention.

In acute poisoning, in addition to gastric lavage, supportive measures should be employed. The blood pressure may be maintained by giving 5% glucose intravenously. Injections of 10% calcium gluconate have been reported to be effective in the relief of the epigastric pain and recurrent vomiting. Complications must be treated symptomatically. To avoid liver damage high carbohydrate and high calcium diet is recommended.

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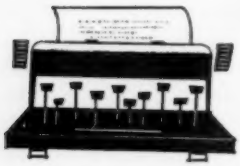
(This is the fourteenth of a series of papers by Dr. Jacobziner)



Books...

Authors' Summaries...

Edited by

MICHAEL A. BRESCIA, M.D.

Poliomyelitis: Papers and Discussions Presented at the Fifth International Poliomyelitis Conference. Copenhagen, Denmark, July 26-28, 1960. J. B. Lippincott Company, Philadelphia, 1961. $7.50.

The two general subjects of this conference were first, Virology and second, Poliomyelitis vaccines. Previous conferences having devoted much time and space to the discussion of the care of patients, the social effects of the disease and to physical medicine, these subjects were not included at this time.

Under the first subject, Virology, some sixteen papers discussed such aspects as morphology, mutations, virus reproduction, cell responses and the like. Under the second subject, poliomyelitis vaccines, there were fourteen papers on inactivated vaccines, their protective efficacy, duration of immunity, and recent developments. On attenuated virus vaccines, there were seventeen papers discussing such subjects as experience in field safety and efficiency, antibody response, dosage and regimen, and the effect on the community.

The information uncovered was exhaustive, and the viewpoints expressed were numerous. Fortunately, there is a nice one-and-a-quarter page summary of the conference by Dr. Frank L. Horsfall, Jr. Under Virology he mentioned the reports and remarkable discoveries bearing on viral structure, composition and function as well as the identification of nucleic acids with viral inheritance. As to the vaccines he noted that the protectiveness of the inactivated vaccines against paralytic poliomyelitis "has reached up and even beyond 95 percent." He has no doubt that when fed to vast numbers of human beings certain attenuated strains of poliomyelitis do not induce disease, but adds that the chief question that remains is how effective attenuated vaccine will be in preventing paralytic poliomyelitis. Studies of antibody level should provide answers for which vaccine to use and how. He concluded with the statement, "Means for the control of poliomyelitis appear to be at hand."

This book is obviously a "must" for all profound students of the causation and prevention of poliomyelitis.

PHILIP M. STIMSON, M.D.

"Birth Injuries of the Newborn", PHILIP SCHWARTZ, M.D. Pp. 384. Ill. 100. Hafner Publishing Company, New York, 1961. $19.50.

The author, an outstanding pathologist, has been interested in birth injuries for four decades, and has done fundamental work in this field, thereby decidedly influencing our pertinent concepts and shedding light on the heretofore incompletely understood pathogenesis of findings in the brain of the newborn. His experiences and old and recent views are excellently expounded in this impressive and beautifully illustrated volume.

Schwartz emphasizes the frequency of cerebral hemorrhages and softenings, the regular involvement of the Galenic venous system, and the significance of pressure differences between uterine contents and atmosphere during the birth process after rupture of the membranes. These subjects he has dealt with in his early papers, and has furnished convincing evidence of the great pathogenetic role of mechanical factors. In addition to atmospheric suction, displacements and movements of cranial bones, fluctuations of intrauterine hypostatic pressure, and asphyxia from various causes, may produce cerebral lesions through vasomotor disturbances. Points of practical interest like the importance of birth lesions in the development of cerebo-spinal deformities, epilepsy, cerebral palsy and mental retardation are elaborated; the significance of prematurity is discussed; and it is stated that care for pregnant women may often prevent premature delivery and birth lesions.

The book is particularly readable since the main text is concise, and, including the illustrations, occupies scarcely 100 pages. A useful supplement is furnished in the annotations, where the literature is thoroughly and critically reviewed, and a wealth of additional information is found. The bibliography is as complete as humanly possible. Annotations and bibliography together occupy more than two-thirds of the book. One may, perhaps, take exception to the use of old drawings and photographs, some of them from the author's previous communications; however, this reviewer cannot think of any better illustrations of the topics under consideration. The index, while complete and detailed, would be easier to use if it were arranged in alphabetical order. A delightful foreword by Sir Eardley Holland introduces the work. The value of the book for pathologists, obstetricians, neurologists, and especially for pediatricians, can hardly be overstated.

KARL T. NEUBUERGER, M.D.

Pathology of Infancy and Childhood By AGNES R. MACGREGOR, M.D., F.R.C.P.E., F.R.C.O.G. Cloth. Illustrated. Pp. 631. Price $14.50. E. & S. Livingstone, Ltd. London 1960. U. S. Agents, The Williams and Wilkins Co., Baltimore.

This volume is not an exhaustive text nor as detailed as some other similarly titled volumes. It does, however, have a great deal of merit, its greatest appeal being to the medical student and those embarking on a pediatric career. The book is abundantly and well illustrated, which in no small measure enhances its value. The author divides her book into nine parts, the first of which considers the pathology of the fetal and neonatal periods. Subsequent parts consider developmental malformations, infective diseases, collagen diseases, diseases of metabolism and nutrition, accidental injuries and poisoning, neoplastic diseases, diseases of the blood and finally, miscellaneous diseases in which are considered some of the skin, and the nervous and locomotor systems. M. A. B.

Recent Advances in Human Nutrition, With Special Reference to Clinical Medicine, by J. F. BROCK, M.D., Pages 454, Cloth. Little, Brown and Co., Boston, Mass., 1961. Price $11.50.

This textbook is a comprehensive work on human nutrition. It emphasizes the principles of nutrition as applied to clinical medicine. The book is written in a concise and authoritative manner, with a clarity of expression and in a simple style for easy reading. The author refers to nutritional experiments on animals when they are apparently relevant to the problems of man. There are 14 contributors of international reputation on nutrition and a chapter is presented by the United Nations Agencies on nutritional investigations in the various European and Aso-African countries.

The volume represents and clinically summarizes up-to-date accepted information, scientific and clinical thought on nutrition in health and in disease with an international flavor. There are 35 illustrations with experimentations. This volume is prepared especially for the information of medical practitioners who do not have time to keep abreast of the very large literature in nutritional science, but who are interested in its relevance to medical practice. The book is valuable to pediatricians, internists and dieticians. An excellent informative book for your library.

JOSEPH M. COVELLI, M.D.

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IN INFANT COLIC... PATHILON® PEDIATRIC DROPS

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1. Kane, S.: Am. Pract. & Digest Treat. *8*:65 (Jan.) 1957.

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